

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method for the production of an aromatic or hetroaromatic fluorine-labelled compound comprising fluoridation of an iodonium salt of Formula (I) or (II):



wherein:

Q is an electron deficient aromatic or heteroaromatic moiety;

each of R¹, R², R³, R⁴ and R⁵ is independently hydrogen, -O(C₁₋₁₀ alkyl) or C₁₋₁₀ alkyl or protected versions thereof; and

Y⁻ is a counter ion such as trifluoromethane sulfonate (triflate), perfluoro C₂-C₁₀ alkyl sulphonate, trifluoroacetate, methane sulfonate (mesylate), toluene sulfonate. (tosylate), tetraphenylborate;

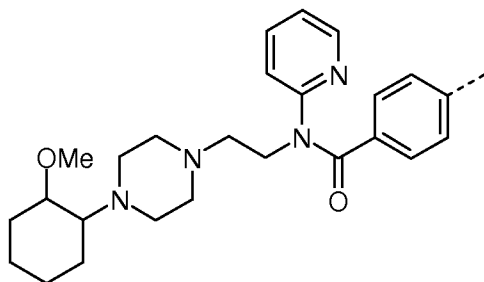
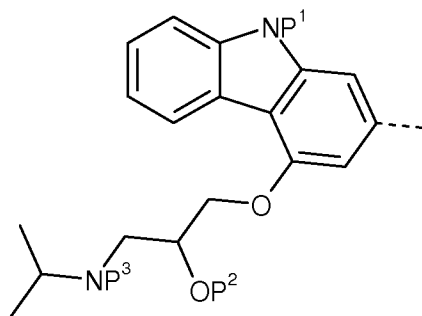
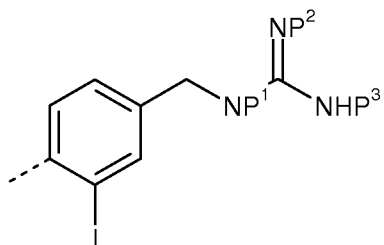
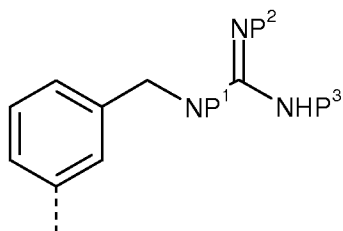
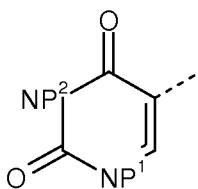
to give a product of general formula (III):

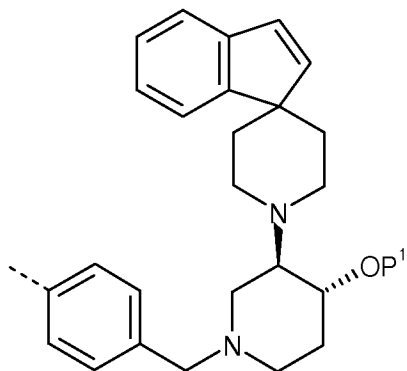
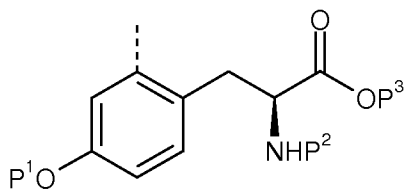
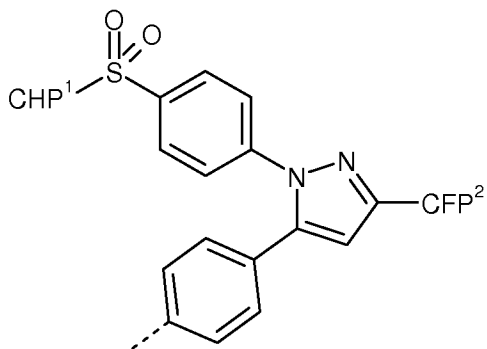
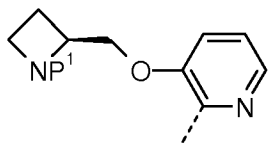
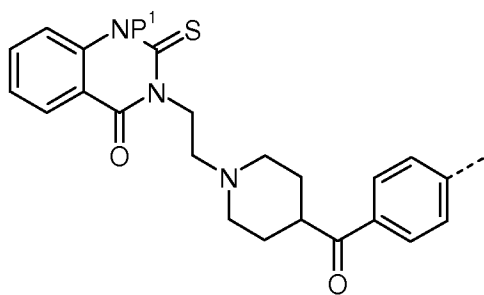


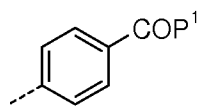
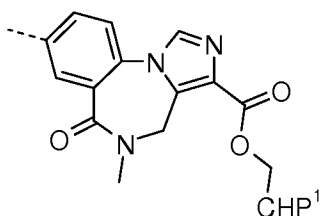
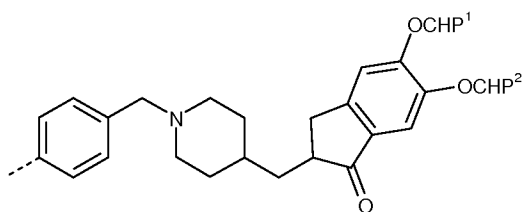
where Q is substituted with one or more substituents selected from C₁₋₁₀ alkyl, -O(C₁₋₁₀ alkyl), -C(=O) C₁₋₁₀ alkyl, -C(=O)NR⁶(C₁₋₁₀ alkyl), -(C₁-C₆ alkyl)-O-(C₁-C₆ alkyl), C₅₋₁₄ aryl, -O(C₅₋₁₄ aryl), -C(=O)C₅₋₁₄ aryl, -C(=O)NR⁶(C₅₋₁₄ aryl, C₅₋₁₄ heteroaryl, -O(C₅₋₁₄ heteroaryl), -C(=O)C₅₋₁₄ heteroaryl, -C(=O)NR⁶(C₅₋₁₄ heteroaryl), C₃₋₁₀ cycloalkyl, -O(C₃₋₁₀ cycloalkyl), -C(=O)(C₃₋₁₀ cycloalkyl), -C(=O)NR⁶(C₃₋₁₀ cycloalkyl), C₃₋₁₀ heterocyclyl, -O(C₃₋₁₀ heterocyclyl), -C(=O)(C₃₋₁₀ heterocyclyl), -C(=O)NR⁶(C₅₋₁₄ heterocyclyl) or protected versions thereof, when Q is substituted with an electron donating substituent, Q also contains one or more electron withdrawing groups to ensure Q is electron deficient;
and wherein said fluoridation is carried out with a fluoride ion source characterised in that the reaction solvent is either 100% water or a mixture of water and a water miscible solvent.

2. (Cancelled)
3. (Cancelled)
4. (Previously presented) A method as claimed in claim 1, wherein the water miscible solvent is acetonitrile, ethanol, methanol, tetrahydrofuran or dimethylformamide.
5. (Previously Presented) A method as claimed in claim 1 wherein the volume:volume ratio of water:water-miscible solvent is between 1:99 and 1:1.
6. (Original) A method as claimed in claim 5 wherein the volume:volume ratio of water:water-miscible solvent is from 10:90 to 30:70.
7. (Previously Presented) A method as claimed in claim 1, wherein the fluoride ion source is potassium, caesium or sodium fluoride.
8. (Cancelled)

9. (Previously Presented) A method as claimed in claim 1, wherein each of R^1 - R^5 is independently selected from hydrogen, C_{1-3} alkyl and $-O-(C_{1-3}$ alkyl).
10. (Previously Presented) A method as claimed in claim 1 wherein, in the compound of Formula II, the "solid support" is polystyrene, polyacrylamide, polypropylene or glass or silicon coated with such a polymer.
11. (Previously Presented) A method as claimed in claim 1 wherein the solid support is in the form of small discrete particles or is a coating on the inner surface of a reaction vessel.
12. (Previously Presented) A method as claimed in claim 1, wherein, in the compound of Formula II the "linker" is C_{1-20} alkyl or C_{1-20} alkoxy, attached to the resin by an amide ether or a sulphonamide bond or a polyethylene glycol (PEG) linker.
13. (Previously Presented) A method as claimed in claim 1
wherein R^6 is H, C_1 - C_6 alkyl, C_3 - C_{10} cycloalkyl, C_3 - C_{10} heterocyclyl, C_4 - C_{10} aryl or C_4 - C_{10} heteroaryl;
any of which may optionally be substituted with OH, NHR^6 , COOH or protected versions
any of these groups; or alternatively
any two adjacent substituents may form a four- to six-membered carbocyclic or heterocyclic ring, optionally fused to a further aromatic, heteroaromatic, carbocyclic or heterocyclic ring.
14. (Previously Presented) A method as claimed in claim 1, wherein the aromatic moiety Q has an additional substituent selected from OH, NHR^6 or halogen.
15. (Currently amended) A method as claimed in claim 1, wherein the group Q is substituted with an electron donating substituent, Q also contains one or more electron withdrawing groups to ensure Q is electron deficient and is one of the following:



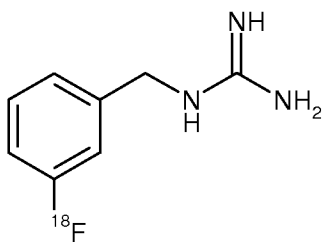
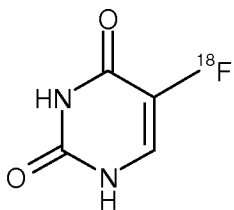


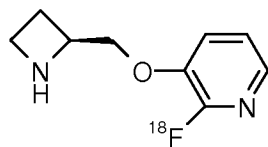
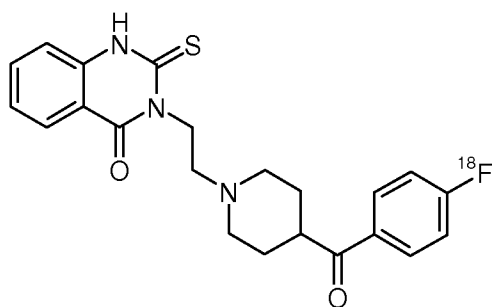
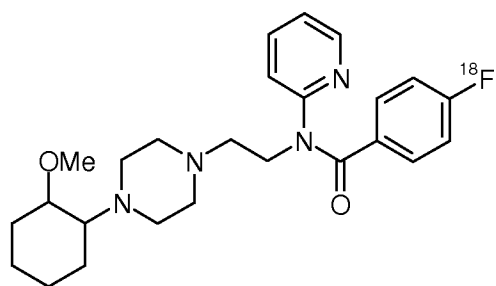
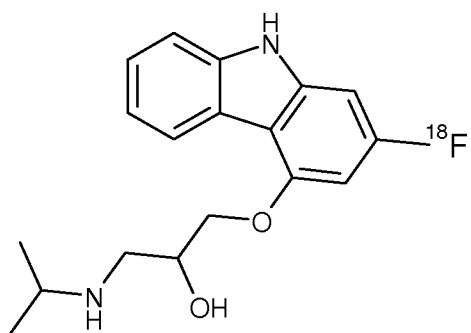
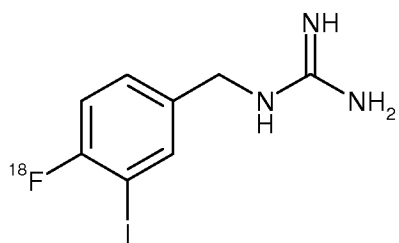


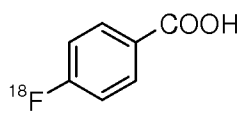
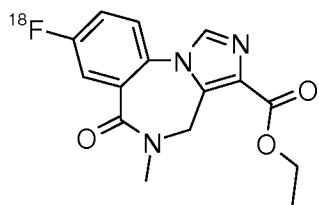
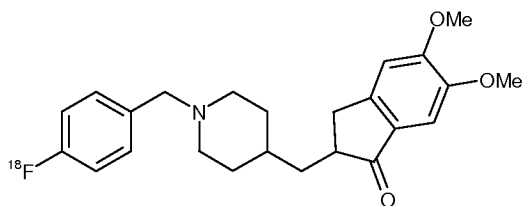
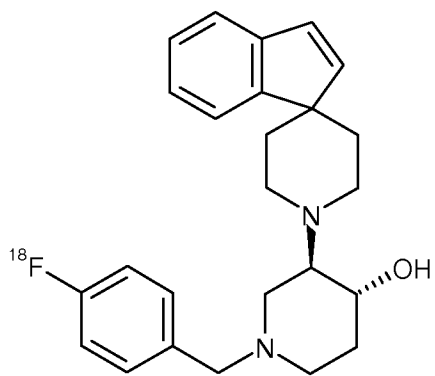
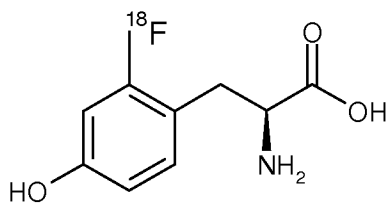
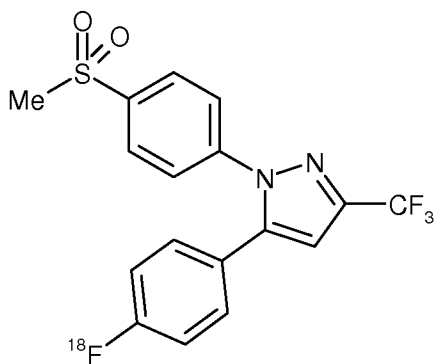
wherein P1 to P3 are either independently hydrogen or a protecting group.

16. (Previously Presented) A method as claimed in claim 1, wherein the fluorine-labelled compound is an [^{18}F]-labelled compound and the fluoride ion source is a source of $^{18}\text{F}^-$.

17. (Currently amended) A method as claimed in claim 1, wherein Q is substituted with an electron donating substituent, Q also contains one or more electron withdrawing groups to ensure Q is electron deficient and further wherein the F-labelled compound is selected from the following:







18. (Previously Presented) A method as claimed in claim 1, further including, in any order, one or more of the following steps: removal of excess $^{18}\text{F}^-$, for example by ion-exchange chromatography; and/or

- (i) removal of the protecting groups; and/or
- (ii) removal of organic solvent; and/or
- (iii) formulation of the resultant compound as an aqueous solution.

19. (Currently amended) A kit for the production of an aromatic fluorine-labelled compound, the kit comprising:

- (i) a vial containing an aqueous solvent for dissolving the fluoride ion source; and
- (ii) a reaction vessel containing an iodonium salt of claim 1.

20. (Original) A kit as claimed in claim 19, wherein the solvent is 100% water.

21. (Original) A kit as claimed in claim 19 wherein the solvent is a mixture of water and a water miscible solvent.

22. (Original) A kit as claimed in claim 21, wherein the water miscible solvent is acetonitrile, ethanol, methanol, tetrahydrofuran or dimethylformamide.

23. (Previously Presented) A kit as claimed in claim 21 wherein the volume:volume ratio of water:water-miscible solvent is between 1:99 and 1:1.

24. (Original) A kit as claimed in claim 23 wherein the volume:volume ratio of water:water-miscible solvent is from 10:90 to 30:70.

25. (Currently amended) A kit as claimed in claim 19 wherein the iodonium salt is compound of ~~general~~ formula (I) or (II) wherein



further wherein:

Q is an electron deficient aromatic or heteroaromatic moiety;

each of R¹, R², R³, R⁴ and R⁵ is independently hydrogen, -O(C₁₋₁₀ alkyl) or C₁₋₁₀ alkyl; and

Y⁻ is a counter ion such as trifluoromethane sulfonate (triflate), perfluoro C₂-C₁₀ alkyl sulphonate, trifluoroacetate, methane sulfonate (mesylate), toluene sulfonate. (tosylate), tetraphenylborate;

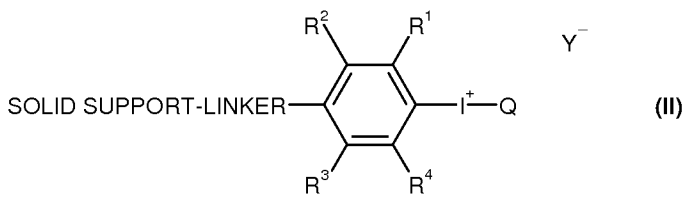
to give a product of general formula (III):



where Q is substituted with one or more substituents selected from C₁₋₁₀ alkyl, -O(C₁₋₁₀ alkyl), -C(=O) C₁₋₁₀ alkyl, -C(=O)NR⁶(C₁₋₁₀ alkyl), -(C₁-C₆ alkyl)-O-(C₁-C₆ alkyl), C₅₋₁₄ aryl, -O(C₅₋₁₄ aryl), -C(=O)C₅₋₁₄ aryl, -C(=O)NR⁶(C₅₋₁₄ aryl, C₅₋₁₄ heteroaryl, -O(C₅₋₁₄ heteroaryl), -C(=O)C₅₋₁₄ heteroaryl, -C(=O)NR⁶(C₅₋₁₄ heteroaryl), C₃₋₁₀ cycloalkyl, -O(C₃₋₁₀ cycloalkyl), -C(=O)(C₃₋₁₀ cycloalkyl), -C(=O)NR⁶(C₃₋₁₀ cycloalkyl), C₃₋₁₀ heterocyclyl, -O(C₃₋₁₀ heterocyclyl), -C(=O)(C₃₋₁₀ heterocyclyl), -C(=O)NR⁶(C₅₋₁₄ heterocyclyl) wherein, when Q is substituted with an electron donating substituent, Q also contains one or more electron withdrawing groups to ensure Q is electron deficient;

and wherein said fluoridation is carried out with a fluoride ion source characterised in that the reaction solvent is either 100% water or a mixture of water and a water miscible solvent.

26. (Currently amended) A kit as claimed in claim 20 wherein the iodonium salt is a compound of ~~general~~ formula (II) and the solid support comprises a coating on the surface of the reaction vessel wherein



further wherein:

Q is an electron deficient aromatic or heteroaromatic moiety;

each of R¹, R², R³, R⁴ and R⁵ is independently hydrogen, -O(C₁₋₁₀ alkyl) or C₁₋₁₀ alkyl; and

Y⁻ is a counter ion such as trifluoromethane sulfonate (triflate), perfluoro C₂-C₁₀ alkyl sulphonate, trifluoroacetate, methane sulfonate (mesylate), toluene sulfonate. (tosylate), tetraphenylborate;

to give a product of general formula (III):



where Q is substituted with one or more substituents selected from C₁₋₁₀ alkyl, -O(C₁₋₁₀ alkyl), -C(=O) C₁₋₁₀ alkyl, -C(=O)NR⁶(C₁₋₁₀ alkyl), -(C₁-C₆ alkyl)-O-(C₁-C₆ alkyl), C₅₋₁₄ aryl, -O(C₅₋₁₄ aryl), -C(=O)C₅₋₁₄ aryl, -C(=O)NR⁶(C₅₋₁₄ aryl, C₅₋₁₄ heteroaryl, -O(C₅₋₁₄ heteroaryl), -C(=O)C₅₋₁₄ heteroaryl, -C(=O)NR⁶(C₅₋₁₄ heteroaryl), C₃₋₁₀ cycloalkyl, -O(C₃₋₁₀ cycloalkyl), -C(=O)(C₃₋₁₀ cycloalkyl), -C(=O)NR⁶(C₃₋₁₀ cycloalkyl), C₃₋₁₀ heterocyclyl, -O(C₃₋₁₀ heterocyclyl), -C(=O)(C₃₋₁₀ heterocyclyl), -C(=O)NR⁶(C₅₋₁₄ heterocyclyl) wherein, when Q is substituted with an electron donating substituent, Q also contains one or more electron withdrawing groups to ensure Q is electron deficient;

and wherein said fluoridation is carried out with a fluoride ion source characterised in that the reaction solvent is either 100% water or a mixture of water and a water miscible solvent.

27. (Previously Presented) A kit as claimed in claim 19, wherein the reaction vessel is a cartridge or a microfabricated vessel.

28. (Previously Presented) A kit as claimed in claim 19, further comprising a source of fluoride ions.